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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/021,002	12/19/2001	Wei-Wu He	PF150D2	9797

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EXAMINER	
DAVIS, MINH TAM B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/021,002	HE ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 41-64 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 41-64 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The finality of the previous Office action has been withdrawn, and the prosecution of this application is reopened to include rejections not previously cited.

It is noted that applicant has paid for a Notice of Appeal. Applicant can either request a refund or place the funds on credit for future appeals.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 41-64 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 101, UTILITY, NEW REJECTION

35 U.S.C. 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 41-64 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility.

Claims 41-64 are drawn to:

A method for detecting PSR protein in a biological sample, comprising detecting the binding of said PSR protein to an antibody or fragment thereof that specifically binds

to a protein consisting of amino acid residues 1 to 316 of SEQ ID NO:2, or to a protein whose amino acid sequence consists of the mature polypeptide encoded by the cDNA contained in ATCC deposit number 75913 (Claims 41, 53).

The method of claim 41, wherein the antibody or fragment thereof is a polyclonal, monoclonal, chimeric, humanized, or single chain antibody, or a Fab fragment (claims 42-44, 54-56).

The method of claim 41, wherein the antibody or fragment thereof is labeled (claims 45-46, 57-58).

The method of claim 41, wherein the biological sample is tissue, cell, plasma, serum, saliva or urine (claims 47-52, 59-64).

The specification discloses a human prostatic specific reductase cDNA, sometime referred as PSR (p.1, last line of paragraph 0002), encoding a protein of 316 amino acids of SEQ ID NO:2 (figure 1).

The specification further discloses that three prostatic libraries are constructed and large number of clones from these libraries are sequenced, i.e. 4472 clones from normal prostate, 956 clones from stage B2 prostate cancer, 3397 clones from stage C prostate cancer, and 275, 261 clones from all other tissues (p.11, paragraph 0056). The specification discloses that the clones identified in these libraries are compared with a database which contains 275,261 independent cDNA clone identifications obtained from more than 300 human cDNA libraries other than human prostatic cDNA libraries (p.11, paragraph 0057). The specification discloses that as shown in table 1 on page 11 that the control PSA is detected 4 times in normal prostate as compared to 7 and 14 times in

prostate cancer, and zero time in all other tissues. The specification discloses that the claimed PSR gene is found zero time in normal prostate, and all other tissues, but is found 3 and 7 times in prostate cancer.

The specification discloses that the claimed prostatic specific reductase is homologous to other reductases, the oxidoreductase and fvt1, with boxed amino acids corresponding exactly between the polypeptides (Figure 2 legend on page 5).

Based on sequence similarity search, SEQ ID NO:2 is 87% similar to a mouse oxidoreductase (MPSRCH search report, 2004, us-10-021-002-2.rup, page 9), and 95% similar to a prostate short-chain dehydrogenase reductase 1 (MPSRCH search report, 2004, us-10-021-002-2.rup, pages 1-2).

The specification contemplates diagnosing prostate cancer metastasis, using the claimed polynucleotide sequence, and treating prostate cancer, using antagonists to the encoded polypeptide thereof (p.3, last paragraph, bridging p. 4)

A. However, neither the specification nor any art of record teaches what SEQ ID NO:2 is, what it does do; they do not teach a utility for any of the fragments claimed; they do not teach a relationship to any specific diseases or establish any involvement in the etiology of any specific diseases. The asserted utilities for SEQ ID NO:2, such as production of and screening of agonists, antibodies and antagonists apply to many unrelated polypeptide structures sequences. Therefore the asserted utilities are not considered "specific" utilities, i.e. they are not specific to SEQ ID NO:2. Additional disclosed utilities for SEQ ID NO:2 include therapy and diagnosis of conditions and diseases characterized by expression of SEQ ID NO:2. The asserted utility of SEQ ID

NO:2 is based on the assertion that that the claimed PSR gene encoding the PSR protein SEQ ID NO:2 is found zero time in normal prostate, and all other tissues, but is found 3 and 7 times in prostate cancer.

It is noted that 956, 4472 and 3397 sequenced clones for use the identification of the number of times the PSR sequence is present in said individual pool of clones, in table 1, on page 11 of **the claimed invention would not be representative of the expressed mRNAs in a cell**, because a complete cDNA library is one that contains at least one cDNA clone representing each mRNA in a cell, and that there are about 34,000 different types of mRNAs in a mammalian cells and about 500,000 mRNA molecules per cell, as taught in a commonly used text book by Ausubel et al, eds, 1987 (Current protocols in molecular biology, John Wiley & Sons, New York, p. 5.8.1, under Production of a cDNA library, of record). Ausubel et al further teach that if the number of molecules of the rarest mRNA in a cell is 8, the calculated number of clones that should be screened to achieve a 99% probability that a cDNA will exist in the library is 324,000. Similarly, in another commonly used text book by Sambrook et al, eds, 1989 (Molecular cloning, a Laboratory manuall, 2nd ed, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, p.8.3-8.7, of record) Sambrook et al teach that a typical mammalian cell contains between 10,000 and 30,000 different mRNA sequences. Sambrook et al further teach that for low abundance mRNAs, i.e. 14 copies/cell, although the minimum clones required to obtain representation of mRNAs of this class is 37,000, but because of preferential cloning of certain sequences, a much larger number of recombinants must be obtained to increase the chances that any given clone will be represented in

the library, i. e., about 170,000 clones (p.8.5 last paragraph, bridging p.8.7). Sambrook et al also teach that unfortunately, many mRNAs of interest are present at even lower level, i.e. 1 molecule/cell is not unusual. Thus based on the teaching in the art, it is clear that the number of the sequenced clones for use in the identification of the number of times the PSR sequence is present in the claimed invention would not be representative of all mRNAs present in a cell.

The identification of the polynucleotide encoding the polypeptide of SEQ ID NO:2 in prostate cancer but not normal libraries in the selected, incomplete pool of sequenced clones appears to be a serendipitous event. The fact that the claimed polynucleotide is not expressed in one pool of sequenced clones or is expressed in another appears to be an artifact of the analytical system and cannot be extrapolated to a prediction of whether that molecule is expressed in the tissue "represented" by the library.

It is not possible to determine from the information in the specification whether SEQ ID NO:2 is overexpressed in prostate cancer tissues as compared to normal prostate tissues, and further experimentation is required to determine whether the claimed method could be used for detecting prostate cancer.

Further, although the specification discloses some homology between SEQ ID NO:2 and the two reductases, oxidoreductase and fvt1, and their sequence alignment, with stretches of exact amino acids between the polypeptides boxed, **the specification does not teach whether there exist and/or which consensus or conserved sequences, that are required for the reductase activity of the encoded protein.**

It is clear however that, although there is an 87% or 95% identity between SEQ ID NO:2 and an oxidoreductase or a short-chain dehydrogenase reductase 1, there is a 13% or 5%, respectively, dissimilarity between SEQ ID NO:2 and an oxidoreductase or a short-chain dehydrogenase reductase 1; and the effects of these dissimilarities upon protein structure and function cannot be predicted. Skolnick et al (Trends in Biotechnology 18: 34-39, 2000, of record) disclose that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the abstract; and page 34, Sequence-based approaches to function prediction). Skolnick et al state that "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Box 2, page 36). Bowie et al (Science, 1990, 257:1306-1310, of record) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are

critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). In addition, Bork (Genome Research, 2000,10:398-400, of record) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3). Furthermore, recent studies show that alternative splicing might affect more than 30% of human genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at protein level is enormous. Each of these modifications may change the function of respective gene products drastically (p. 399, col 1). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, col 2). Most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399 para bridging cols 2 and 3). The

reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those feature are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, para bridging cols 1 and 2). Further, Scott et al (Nature Genetics, 1999, 21:440-443, of record) teach that the gene causing Pendred syndrome encodes a putative transmembrane protein designated pendrin. Based on sequence similarity data, the authors postulated that the putative protein was deemed to be a member of sulfate transport proteins that included a 29% identity to rat sulfate-anion transporter, 32% similarity to human diastrophic dysplasia sulfate transporter, and 45% similarity to the human sulfate transporter "downregulated in adenoma". However, upon analyzing the expression and kinetics of the protein, the data revealed no evidence of sulfate transport wherein results revealed that pendrin functioned as a transporter of chloride and iodide. Scott et al. suggest that these results underscore the importance of confirming the function of newly identified gene products even when the database searches reveal significant homology to proteins of known function (page 411, 1st column, 4th paragraph). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250, of record) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there

are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Clearly, given not only the teachings of Skolnick et al, Bowie et al, and Scott et al, Doerks et al, but also the limitations and pitfalls of using computational sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function as taught by Bork, with a 13% or 5% dissimilarity to an oxidoreductase or a short-chain dehydrogenase reductase 1, respectively, the function of the predicted encoded SEQ ID NO:2 could not be predicted, based on sequence similarity with an oxidoreductase, or a short-chain dehydrogenase reductase 1, nor would it be expected to be the same as that of an oxidoreductase or a short-chain dehydrogenase reductase 1.

Thus, neither the specification nor any art of record teaches what the PSR protein of SEQ ID NO:2 is, what it does do; they do not teach a relationship to any specific diseases or establish any involvement in the etiology of any specific diseases.

The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

B. In the reply of 09/23/05, Applicant asserts that the enzymatic reductase activity of PSR is specific, substantial and credible. Applicant asserts that SEQ ID NO:2 is 98% similar to the short-chain dehydrogenase/reductase PSDR1 by Lin et al, 2001, wherein both contain the conserved segments, GlyXXXGlyXGly, and TyrXXXLys, which

are present in members of the short-chain dehrydrogenase/reductase enzyme family. Applicant asserts that as shown in the provided alignment between SEQ ID NO:2 and the short-chain dehydrogenase/reductase PSDR1 by Lin et al, the minor sequence differences between PSR and PSDR1 do not appear to be at positions conserved amongst the portions of the proteins aligned in figure 2 of Lin et al. Applicant asserts that further, Kedishvili et al, 2003, teach that PSDR1 has reductase activity.

It is noted **that Lin et al, 2001, is a post-filed reference, and that the properties of the specific conserved segments, GlyXXXGlyXGly, and TyrXXXLys, disclosed in Lin et al, i.e. necessary for the binding of NAD(H) or NADP(H) and the activity of the enzyme, respectively, were not disclosed at the time the invention was filed.** In view of a lack of a disclosure of a consensus sequence neccessary for the reductase activity at the time of filing of the instant application, the specification essentially gives an invitation to experiment to determine whether SEQ ID NO:2 is a reductase, and thus the artisan is invited to elaborate a functional use for the disclosed polypeptide.

Further, even if SEQ ID NO:2 belong to the family of short-chain dehrydrogenase/reductase enzymes (SDRs), **one cannot determine the specific function of SEQ ID NO:2, in view of the teaching of Lin et al that SDRs encompass a large group of functionally diverse proteins (Lin et al, 2001, Cancer Res, 61: 1611-1618, especially p. 1615, second column, lines 8-10, under Discussion), and further in view that one cannot determine which compound is the specific substrate for the reductase activity of SEQ ID NO:2.**

There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family. However, this is not the case for the claimed invention as no function has been elucidated for the claimed SEQ ID NO:2, in view of the teaching of Lin et al that SDRs encompass a large group of functionally diverse proteins, supra, and further in view that there is no indication that the family of short-chain dehrydrogenase/reductase enzymes (SDR) has non-specific substrate requirements. This is substantiated by Kedishvili et al, 2003, JBC, 277 (32): 28909-28915, which teaches that PSDR1 requires a specific substrate, i.e. having oxidoreductive catalytic activity toward retinoids, but not steroids (abstract). Further, the relevant literature reports numerous examples of polypeptide families wherein individual members have distinct, and even opposite, biological activities. For example, Tischer et a1. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial' cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occuning PDGF, which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences between PDGF and VEGF are also seen in vivo, wherein endothelial-pericyte associations in the eye are disrupted by intraocular administration of PDGF but

accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598; see Abstract and pp. 1594-1596). Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-/ family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- beta family members BMP-2 and TGF-beta 1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Similarly, PTH and PTHrP are two structurally closely related proteins, which can have opposite effects on bone resorption (Pilbeam et al, 1993, Bone14:717-720; see p. 717, second paragraph of Introduction). Finally, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48).

In view of the above teaching, even if SEQ ID NO:2 belong to the family of short-chain dehrydrogenase/reductase enzymes (SDRs), one cannot determine which compound is the specific substrate for the reductase activity of SEQ ID NO:2, and consequently one cannot determine the specific function and the utility of SEQ ID NO:2.

Further experimentation is required to determine what use is for the claimed SEQ ID NO:2 or the polynucleotide encoding SEQ ID NO:2.

Further, although practical utility can be inferred if each and every member of the broad class possesses a common utility. However, SEQ ID NO: 2 has not been shown to have a common utility with members of the family of short-chain dehrydrogenase/reductase enzymes (SDRs), because one cannot determine the specific function of SEQ ID NO:2, in view of the teaching of Lin et al that SDRs

encompass a large group of functionally diverse proteins (Lin et al, 2001, Cancer Res, 61: 1611-1618, especially p. 1615, second column, lines 8-10, under Discussion), and further in view that one cannot determine which compound is the specific substrate for the reductase activity of SEQ ID NO:2.

For the reasons set forth above, further experimentation is required to determine what use is for the claimed polypeptide or the encoding polynucleotide.

In the absence of any disclosed relationship between the claimed polynucleotide and the encoded polypeptide thereof and any disease or disorder and the lack of any correlation between the claimed polypeptide and the encoding polynucleotide thereof with any known disease or disorder, and further in view that any potential diagnostic or therapeutic utility is not yet known and has not yet been disclosed, the utility is not substantial. Further research is necessary to determine what use is for the claimed polypeptide or the encoding polynucleotide thereof. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPO at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. 101.

For reasons set forth above the disclosure satisfies none of the three criteria of a specific, and substantial utility. *See In re Kirk*, 153 USPO 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as

to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 41-64 are rejected under 35 U.S.C. 112, first paragraph.

1. Specifically, since the claimed invention is not supported by specific, substantial utility or a well established utility for the reasons set forth in the rejection under 35 USC 101 above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments and reasons of rejection from the 101 utility rejection apply here as well.

2. If Applicant could overcome the above 112, first paragraph rejection, Claims 41-64 are still rejected under 112, first paragraph, because the claims encompass a method for detecting PSR variants, for reasons already of record in paper of 05/23/05.

Rejection remains because Applicant did not reply to the rejection.

Even if SEQ ID NO:2 were overexpressed in primary prostate cancer, one cannot predict that the claimed PSR variants would also be overexpressed in prostate cancer, in view of the teaching of Schmid S et al, 2001, and Conner et al, 1996, all of record, that variants do not necessarily express in the same pattern as the wild type parent sequence.

Further, even if SEQ ID NO:2 were a reductase, one cannot predict that the claimed PSR variants would have properties related to that of SEQ ID NO:2 and would be detected by an antibody to SEQ ID NO:2, in view of the teaching of Bowie et al, and Roger et al, all of record, that protein chemistry is unpredictable, and that the unique three-dimensional structure of a protein could be dramatically changed by changing its amino acid composition, and consequently the binding and characteristics of the antibodies for said protein.

3. If Applicant could overcome the above 112, first paragraph rejection, Claims 41-64 are still rejected under 112, first paragraph, because the claims encompass a method for detecting prostate specific reductase (PSR) using any

biological sample, any tissue or any cells or saliva, i.e. a method for detecting PSR in metastatic prostate cells, which have metastasized to any sample, tissue, cell or saliva, for reasons already of record in paper of 05/23/05.

Rejection remains because Applicant did not reply to the rejection.

It is noted that SEQ ID NO:2 is prostate specific.

Even if SEQ ID NO:2 were overexpressed in primary prostate cancer, one cannot predict that metastatic prostate cancer cells still express or overexpress SEQ ID NO:2, in view of the teaching of Zhau et al, Cheung et al, Ren et al and Gingrich et al, all of record, that expression of a sequence could be lost during progression toward metastasis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

MINH TAM DAVIS

January 24, 2006

SUSAN UNGAR, PH.D
PRIMARY EXAMINER